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# AMENDMENTS TO THE CLAIMS

The following listing of claims will replace all prior versions and listings of claims in the application.

## Listing of claims:

Claim 1 (currently amended). A compound selected from those of formula (I):

$$(R_2)_m \xrightarrow{A} (Z_1)_n \xrightarrow{Z} X_3 \xrightarrow{R_1} N \xrightarrow{R_1} W$$

$$(I)$$

in which:

R<sub>1</sub> represents <u>hydrogen</u>, a group selected from:

- hydrogen, amino,
- (C<sub>1</sub>-C<sub>6</sub>)alkyl, (C<sub>2</sub>-C<sub>6</sub>)alkenyl, (C<sub>3</sub>-C<sub>6</sub>)alkynyl, mono(C<sub>1</sub>-C<sub>6</sub>)alkylamino(C<sub>1</sub>-C<sub>6</sub>)alkyl, di(C<sub>1</sub>-C<sub>6</sub>)alkylamino(C<sub>1</sub>-C<sub>6</sub>)alkyl, aryl, aryl(C<sub>1</sub>-C<sub>6</sub>)alkyl, heterocycle, and 3- to 6 membered cycloalkyl(C<sub>1</sub>-C<sub>6</sub>)alkyl, those groups being unsubstituted or substituted with one or more groups, which may be identical or different, selected from amino, (C<sub>1</sub>-C<sub>6</sub>)alkyl, cyano, halo(C<sub>1</sub>-C<sub>6</sub>)alkyl, C(=O)OR<sub>47</sub>-OR<sub>4</sub> and SR<sub>47</sub>-in which R<sub>4</sub>-represents hydrogen or (C<sub>1</sub>-C<sub>6</sub>)alkyl,

W represents an oxygen atom, a sulphur atom, or a group =N-R', in which R' represents ( $C_1-C_6$ )alkyl, hydroxyl, or cyano,

X<sub>1</sub> and X<sub>3</sub> represent, independently of each other, a group -C-R<sub>6</sub> in which R<sub>6</sub> represents a group selected from hydrogen, (C<sub>1</sub>-C<sub>6</sub>)alkyl, amino,

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mono( $C_1$ - $C_6$ )alkylamino, di( $C_1$ - $C_6$ )alkylamino, hydroxyl, ( $C_1$ - $C_6$ )alkoxy, and halogen;

X<sub>2</sub> is nitrogen;

Y represents a group selected from oxygen atom, sulphur atom, -NH, and -N(C<sub>1</sub>-C<sub>6</sub>)alkyl,

#### Z represents:

- an oxygen atom, a sulphur atom,
- or a group -NR<sub>7</sub> in which R<sub>7</sub> represents a group selected from hydrogen,
   (C<sub>1</sub>-C<sub>6</sub>)alkyl, aryl(C<sub>1</sub>-C<sub>6</sub>)alkyl, cycloalkyl, aryl, and heteroaryl, and
- when Y is an oxygen atom, a sulphur atom, or a group  $-N(C_1-C_6)$  alkyl, Z optionally represents a carbon atom which is unsubstituted or substituted with a  $(C_1-C_6)$  alkyl, an aryl, an aryl $(C_1-C_6)$  alkyl, an aromatic or non-aromatic heterocycle or a cycloalkyl,

n is an integer from 1 to 8 inclusive,

 $Z_1$  represents  $-CR_8R_9$  wherein  $R_8$  and  $R_9$ , independently of each other, represent a group selected from hydrogen,  $(C_1-C_6)$ alkyl, halo $(C_1-C_6)$ alkyl, halogen, amino,  $OR_4$ ,  $SR_4$  or  $C(=O)OR_4$  in which  $R_4$  represents a hydrogen or  $(C_1-C_6)$ alkyl, and

- when n is greater than or equal to 2, the hydrocarbon chain  $Z_1$  optionally contains one or more multiple bonds,
- and/or one of the carbon atoms in the hydrocarbon chain Z<sub>1</sub> may be replaced with an oxygen atom, a sulphur atom which is unsubstituted or substituted with one or two oxygen atoms, or a nitrogen atom which is unsubstituted or substituted with a (C<sub>1</sub>-C<sub>6</sub>)alkyl,
- and when one of the carbon atoms in the hydrocarbon chain  $Z_1$  is replaced with a sulphur atom which is unsubstituted or substituted with one or two oxygen

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atoms, then the group -C(=Y)-Z- optionally may be absent in the general formula (I),

A represents an a group selected from:

- aromatic or non-aromatic, 5- or 6-membered monocycle comprising from 0
   to 4 heteroatoms selected from nitrogen, oxygen and sulphur, and
- bicycle, composed of two-aromatic or non-aromatic, 5 or 6 membered rings, which may be identical or different, comprising from 0 to 4 heteroatoms selected from nitrogen, exygen and sulphur,

m is an integer from 0 to 7 inclusive,

the group(s)  $R_2$ , which may be identical or different, is (are) selected from  $(C_1-C_6)$ alkyl, halogen, -CN, NO<sub>2</sub>, SCF<sub>3</sub>, -CF<sub>3</sub>, -OCF<sub>3</sub>, -NR<sub>10</sub>R<sub>11</sub>, -OR<sub>10</sub>, -SR<sub>10</sub>, SOR<sub>10</sub>, -SO<sub>2</sub>R<sub>10</sub>, -(CH<sub>2</sub>)<sub>k</sub>SO<sub>2</sub>NR<sub>10</sub>R<sub>11</sub>, -X<sub>5</sub>(CH<sub>2</sub>)<sub>k</sub>C(=O)OR<sub>10</sub>, -(CH<sub>2</sub>)<sub>k</sub>C(=O)NR<sub>10</sub>R<sub>11</sub>, -(CH<sub>2</sub>)<sub>k</sub>C(=O)NR<sub>10</sub>R<sub>11</sub>, and -X<sub>4</sub>-R<sub>12</sub> in which:

- X<sub>5</sub> represents a group selected from oxygen, sulphur optionally substituted by one or two oxygen atoms, and nitrogen substituted by hydrogen or (C<sub>1</sub>-C<sub>6</sub>)alkyl,
  - k is an integer from 0 to 3 inclusive,
- $R_{10}$  and  $R_{11}$ , which may be identical or different, are selected from hydrogen and  $(C_1-C_6)$  alkyl,
- X<sub>4</sub> represents a group selected from single bond, -CH<sub>2</sub>-, oxygen atom, sulphur atom optionally substituted by one or two oxygen atoms, and nitrogen atom substituted by hydrogen atom or (C<sub>1</sub>-C<sub>6</sub>)alkyl group,

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• R<sub>12</sub> represents an aromatic or non-aromatic, heterocyclic or non-heterocyclic, 5- or 6-membered ring which is unsubstituted or substituted with one or more groups, which may be identical or different, selected from (C<sub>1</sub>-C<sub>6</sub>)alkyl, halogen, hydroxyl and amino, and when the ring is heterocyclic, it comprises from 1 to 4 heteroatoms selected from nitrogen, oxygen and sulphur,

## R<sub>3</sub> represents a group selected from:

- hydrogen,
- (C<sub>1</sub>-C<sub>6</sub>)alkyl, (C<sub>2</sub>-C<sub>6</sub>)alkenyl, (C<sub>2</sub>-C<sub>6</sub>)alkynyl, these groups being unsubstituted or substituted with one or more groups, which may be identical or different, selected from amino, cyano, halo(C<sub>1</sub>-C<sub>6</sub>)alkyl, cycloalkyl, C(=O)NR<sub>10</sub>R<sub>14</sub>, C(=O)OR<sub>10</sub>, OR<sub>10</sub>, and SR<sub>10</sub>, in which R<sub>10</sub> and R<sub>14</sub>, which may be identical or different, represent hydrogen or (C<sub>1</sub>-C<sub>6</sub>)alkyl,
  - and the group of formula:

$$(R_5)_q$$
  $(Z_2)_p$ 

- ✓ in which p is an integer from 0 to 8 inclusive,
- ✓ Z<sub>2</sub> represents -CR<sub>13</sub>R<sub>14</sub> wherein R<sub>13</sub> and R<sub>14</sub>, independently of each other, represent a group selected from hydrogen, (C<sub>1</sub>-C<sub>6</sub>)alkyl, phenyl, halo(C<sub>1</sub>-C<sub>6</sub>)alkyl, halogen, amino, OR<sub>4</sub>, SR<sub>4</sub> and -C(=O)OR<sub>4</sub> in which R<sub>4</sub> represents hydrogen or (C<sub>1</sub>-C<sub>6</sub>)alkyl, and
  - when p is greater than or equal to 2, the hydrocarbon chain Z<sub>2</sub> optionally contains one or more multiple bonds,
  - and/or one of the carbon atoms in the hydrocarbon chain Z<sub>2</sub> may be replaced with an oxygen atom, a sulphur atom which is unsubstituted or substituted with one or two oxygen atoms, a nitrogen atom which is unsubstituted or substituted with a (C<sub>1</sub>-C<sub>6</sub>)alkyl, or a carbonyl group,

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- ✓ B represents a group selected from:
  - an aromatic or non-aromatic 5- or 6-membered monocycle comprising from 0 to 4 heteroatoms selected from nitrogen, oxygen and sulphur, and
  - a bicycle, composed of two aromatic or non-aromatic, 5- or 6-membered rings, which may be identical or different, comprising from 0 to 4 heteroatoms selected from nitrogen, oxygen and sulphur,
- ✓ q is an integer from 0 to 7 inclusive,
- ✓ the group(s) R<sub>5</sub>, which may be identical or different, is (are) selected from  $-(CH_2)_kNR_{15}R_{16}$ , CN.  $NO_2$ CF<sub>3</sub>, OCF<sub>3</sub>.  $(C_1-C_6)$ alkyl, halogen,  $-N(R_{15})C(=O)R_{16}$ ,  $-N(R_{15})C(=O)OR_{16}$ ,  $-N(R_{15})SO_2R_{16}$ ,  $-N(SO_2R_{15})_2$ ,  $-OR_{15}$ ,  $-SO_2-N(R_{15})-(CH_2)_{k2}-NR_{16}R_{17}$  $-(CH_2)_kSO_2NR_{15}R_{16}$  $-S(O)_{k1}R_{15}$  $-C(=O)O-(CH_2)_{k2}-NR_{15}R_{16}$  $-X_7(CH_2)_kC(=O)OR_{15}$ ,  $-(CH_2)_kC(=O)OR_{15}$ ,  $-X_7(CH_2)_kC(=O)NR_{15}R_{16}$  $-C(=O)O-(CH_2)_{k2}-C(=O)OR_{18}$ , -(CH<sub>2</sub>)<sub>k</sub>C(=O)NR<sub>15</sub>R<sub>16</sub>, -R<sub>19</sub>-C(=O)OR<sub>15</sub>, -X<sub>6</sub>-R<sub>20</sub>, and -C(=O)- $R_{21}$ -NR<sub>15</sub>R<sub>16</sub> in which:
  - $X_7$  represents a group selected from oxygen atom, sulphur atom optionally substituted by one or two oxygen atoms, and nitrogen atom substituted by a hydrogen atom or a  $(C_1-C_6)$  alkyl group,
  - k is an integer from 0 to 3 inclusive,
  - k1 is an integer from 0 to 2 inclusive,
  - k2 is an integer from 1 to 4 inclusive,

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- $R_{15}$ ,  $R_{16}$  and  $R_{17}$ , which may be identical or different, are selected from hydrogen and  $(C_1-C_6)$ alkyl,
- $R_{18}$  represents a group selected from  $(C_1-C_6)$ alkyl,  $-R_{21}-NR_{15}R_{16}$ ,  $-R_{21}-NR_{15}-C(=O)-R_{21}-NR_{16}R_{17}$ , and  $-C(=O)O-R_{21}-NR_{15}R_{16}$  in which  $R_{21}$  represents a linear or branched  $(C_1-C_6)$ alkylene group, and  $R_{15}$ ,  $R_{16}$  and  $R_{17}$  are as defined hereinbefore,
- R<sub>19</sub> represents a (C<sub>3</sub>-C<sub>6</sub>)cycloalkyl group,
- $X_6$  represents a group selected from single bond, -CH<sub>2</sub>-, oxygen atom, sulphur atom optionally substituted by one or two oxygen atoms, and nitrogen atom substituted by hydrogen atom or (C<sub>1</sub>-C<sub>6</sub>)alkyl group,
- R<sub>20</sub> represents an aromatic or non-aromatic, heterocyclic or non-heterocyclic, 5- or 6-membered ring, which is unsubstituted or substituted with one or more groups, which may be identical or different, selected from (C<sub>1</sub>-C<sub>6</sub>)alkyl, halogen, hydroxyl, oxo, cyano, tetrazole, amino, and -C(=O)OR<sub>4</sub> wherein R<sub>4</sub> represents hydrogen or (C<sub>1</sub>-C<sub>6</sub>)alkyl, and, when the ring is heterocyclic, it comprises from 1 to 4 heteroatoms selected from nitrogen, oxygen and sulphur,

with the provise that when  $X_1$  represents a nitrogen atom,  $X_2$  cannot represent a carbon atom substituted with a methyl group or with NH CH<sub>3</sub>; optionally, the racemic forms thereof, isomers thereof, N-oxides thereof, and the pharmaceutically acceptable salts thereof.

#### Claim 2 (canceled).

Claim 3 (currently amended). A compound of formula (I) according to Claim 1 characterized in that:

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n is an integer from 1 to 6 inclusive,

 $Z_1$  represents  $-CR_8R_9$  wherein  $R_8$  represents a hydrogen atom and  $R_9$  represents a hydrogen atom or a methyl group, and

- when n is greater than or equal to 2, the hydrocarbon chain  $Z_1$  optionally contains a double bond,
- or, one of the carbon atoms in the hydrocarbon chain Z<sub>1</sub> may be replaced with an oxygen atom, or a sulphur atom which is unsubstituted or substituted with one or two oxygens,

A represents a group selected from phenyl, pyridyl, thienyl, imidazolyl, furyl, and piperidyl, 1,3 benzodioxolyl, benzodioxinyl, benzothienyl, benzofuryl, benzofuryl, benzofurazanyl, 2,1,3-benzothiadiazolyl, and indelyl,

m is an integer from 0 to 7 inclusive,

the group(s)  $R_2$ , which may be identical or different, is (are) selected from  $(C_1-C_6) \text{alkyl}, \text{ halogen, -CN, -CF}_3, \text{-OCF}_3, \text{-NR}_{10}R_{11}, \text{-OR}_{10}, \text{-SR}_{10}, \text{-SO}_2R_{10}, \\ \text{-(CH}_2)_k \text{SO}_2 \text{NR}_{10}R_{11}, \text{-X}_5 \text{(CH}_2)_k \text{C} \text{(=O)OR}_{10}, \text{-(CH}_2)_k \text{C} \text{(=O)OR}_{10},$ 

- $-X_5(CH_2)_kC(=0)NR_{10}R_{11}$ ,  $-(CH_2)_kC(=0)NR_{10}R_{11}$ , and  $-X_4-R_{12}$  in which:
- ✓ X<sub>5</sub> represents O, S or NH,
- ✓ k is an integer from 0 to 3 inclusive,
- √ R<sub>10</sub> and R<sub>11</sub>, identical or different, are selected from hydrogen and (C<sub>1</sub>-C<sub>6</sub>)alkyl,
- ✓ X<sub>4</sub> represents -CH<sub>2</sub>-, or an oxygen atom,
- ✓ R<sub>12</sub> represents a phenyl group which is unsubstituted or substituted with one
  or more groups, which may be identical or different, selected from
  (C<sub>1</sub>-C<sub>6</sub>)alkyl, halogen, hydroxyl and amino,

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optionally, the racernic forms thereof, isomers thereof, N-oxides thereof, and the pharmaceutically acceptable salts thereof.

Claim 4 (currently amended). A compound of formula (I) according to Claim 1 characterized in that:

R<sub>3</sub> represents hydrogen, (C<sub>1</sub>-C<sub>6</sub>)alkyl or the group of formula:

$$(R_s)_q$$
  $B$   $(Z_2)_p$ 

- in which p is an integer from 0 to 3 inclusive,
- Z<sub>2</sub> represents -CR<sub>13</sub>R<sub>14</sub> wherein R<sub>13</sub> and R<sub>14</sub>, independently of each other,
   represent a group selected from hydrogen, methyl, or phenyl, and
  - when p is greater than or equal to 2, the hydrocarbon chain Z<sub>2</sub> optionally contains one double bond,
  - or one of the carbon atoms in the hydrocarbon chain Z<sub>2</sub> may be replaced with an oxygen atom, a sulphur atom which is unsubstituted or substituted with one or two oxygen atoms, a nitrogen atom which is unsubstituted or substituted with a (C<sub>1</sub>-C<sub>6</sub>)alkyl, or a carbonyl group,
- B represents a group selected from phenyl, pyridyl, thienyl, imidazolyl, furyl,
   1,3-benzodioxolyl, benzodioxinyl, benzothienyl, benzofuryl,
   2,1,3-benzothiadiazolyl, benzofurazanyl, naphthyl, and indolyl,
- q is an integer from 0 to 3 inclusive,
- the group(s) R<sub>5</sub>, which may be identical or different, is (are) selected from (C<sub>1</sub>-C<sub>6</sub>)alkyl, halogen, CN, NO<sub>2</sub>, CF<sub>3</sub>, OCF<sub>3</sub>, -(CH<sub>2</sub>)<sub>k</sub>NR<sub>15</sub>R<sub>16</sub>,
   -N(R<sub>15</sub>)C(=O)R<sub>16</sub>, -(R<sub>15</sub>)C(=O)OR<sub>16</sub>, -N(R<sub>15</sub>)SO<sub>2</sub>R<sub>16</sub>, -N(SO<sub>2</sub>R<sub>15</sub>)<sub>2</sub>, -OR<sub>15</sub>,
   -S(O)<sub>k1</sub>R<sub>15</sub>, -SO<sub>2</sub>-N(R<sub>15</sub>)-(CH<sub>2</sub>)<sub>k2</sub>-NR<sub>16</sub>R<sub>17</sub>, -(CH<sub>2</sub>)<sub>k</sub>SO<sub>2</sub>NR<sub>15</sub>R<sub>16</sub>,

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$$\begin{split} -X_7(CH_2)_kC(=O)OR_{15}, -(CH_2)_kC(=O)OR_{15}, -C(=O)O-(CH_2)_{k2}-NR_{15}R_{16}, \\ -X_7(CH_2)_kC(=O)NR_{15}R_{16}, \text{ and } -(CH_2)_kC(=O)NR_{15}R_{16} \text{ in which :} \end{split}$$

- X<sub>7</sub> is \$, O or NH,
- k is an integer from 0 to 3 inclusive,
- k1 is an integer from 0 to 2 inclusive,
- k2 is an integer from 1 to 4 inclusive,
- R<sub>15</sub>, R<sub>16</sub> and R<sub>17</sub>, which may be identical or different, are selected from hydrogen and (C<sub>1</sub>-C<sub>6</sub>)alkyl,

optionally, the racemic forms thereof, isomers thereof, N-oxides thereof, and the pharmaceutically acceptable salts thereof.

### Claims 5 to 8 (canceled).

Claim 9 (previously presented). A compound of formula (I) according to

Claim 1 characterized in that:

W represents an oxygen atom,

Y represents an oxygen atom,

Z represents a NH group,

Z<sub>1</sub> represents a methylene group,

and n is equal to one,

optionally, the racemic forms thereof, isomers thereof, N-oxides thereof, and the pharmaceutically acceptable salts thereof.

### Claims 10 and 11 (canceled).

Claim 12 (previously presented). A compound of formula (I) according to Claim 1 characterized in that:

 $X_1$  and  $X_3$  represent each a -CH group, and

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optionally, the racemic forms thereof, isomers thereof, N-oxides thereof, and the pharmaceutically acceptable salts thereof.

Claim 13 (currently amended). A compound of formula (I) according to Claim 1 characterized in that:

A represents a group selected from phenyl, and pyridyl, 1,3 benzedioxolyl, and benzefurazanyl,

m is equal to 0 or 1,

and  $R_2$  represents a group selected from  $(C_1-C_6)$ alkoxy, hydroxy, halogen, and  $(C_1-C_6)$ thioalkoxy,

optionally, the racemic forms thereof, isomers thereof, N-oxides thereof, and the pharmaceutically acceptable salts thereof.

Claim 14 (previously presented). A compound of formula (I) according to Claim 1 characterized in that R<sub>3</sub> represents a group of formula:

$$(R_s)_q$$
  $(Z_2)_p$ 

in which:

p is equal to 1,

 $\mathbb{Z}_2$  represents a methylene group,

B represents a group selected from phenyl, pyridyl, 1,3-benzodioxolyl, and benzofurazanyl,

q is an integer from 0 to 2 inclusive,

and R5 represent(s) a group selected from halogen, CN, -(CH2)kNR15R16,

 $-S(O)_{k1}R_{15}$ ,  $-(CH_2)_kSO_2NR_{15}R_{16}$ ,  $-(CH_2)_kC(=O)OR_{15}$ ,  $-(CH_2)_kC(=O)NR_{15}R_{16}$ , and  $-X_6-R_{20}$ , in which :

- k is an integer from 0 to 1 inclusive,
- k1 is an integer from 0 to 2 inclusive,
- R<sub>15</sub> and R<sub>16</sub>, which may be identical or different, are selected from hydrogen and (C<sub>1</sub>-C<sub>6</sub>)alkyl,

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- X<sub>6</sub> represents a bond,
- -R<sub>20</sub> represents a 5-membered heterocyclic ring comprising from 3 to 4
  heteroatoms selected from oxygen and nitrogen and optionally substituted
  with a methyl group or an oxo group,

optionally, the racemic forms thereof, isomers thereof, N-oxides thereof, and the pharmaceutically acceptable salts thereof.

Claim 15 (currently amended). A compound of formula (I) according to Claim 1, which is:

- 1,3 Dimethyl-2,4-dioxo-1,2,3,4-tetrahydro-pyride[3,4-d]pyrimidine-6-earboxylic acid (1,3-benzodioxol-5-ylmothyl) amide,
- 3-Benzyl-1 methyl-2,4-dioxo 1,2,3,4 tetrahydro pyrido[3,4 d] -pyrimidine 6-carboxylic acid (1,3-benzodioxol-5 ylmethyl) amide,
- Methyl 4-[6-(4-Methoxy-benzylcarbamoyl)-1-methyl-2,4-dioxo-1,4-dihydro-2*H*-pyrido[3,4-*d*]pyrimidin-3-ylmethyl]-benzoate,
- 4-[6-(4-Methoxy-benzylcarbamoyl)-1-methyl-2,4-dioxo-1,4-dihydro-2*H*-pyrido[3,4-*d*]pyrimidin-3-ylmethyl]-benzoic acid,
- 4-[6-(3-Methoxy-benzylcarbamoyl)-1-methyl-2,4-dioxo-1,4-dihydro-2*H*-pyrido[3,4-*d*]pyrimidin-3-ylmethyl]-benzoic acid, and
- 3-(4-Cyano-benzyl)-1-methyl-2,4-dioxo-1,2,3,4-tetrahydro-pyrido[3,4-d]pyrimidine-6-carboxylic acid 4-methoxy-benzylamide.

### Claims 16 to 28 (canceled).

Claim 29 (currently amended). A pharmaceutical composition comprising a compound according to any one of Claims 1, 2, 4, 8, 9, 11-15 Claims 1, 3, 4, 9, or 11-15 inclusive and a pharmaceutically acceptable excipient.

#### Claims 30 and 36 (canceled).

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Claim 37 (currently amended). A method for treating a disease or complaint involving a therapy by inhibition of MMP-13 characterized in that the disease or the complaint is arthritis, the method comprising the administration of an effective amount of a compound according to any one of Claims 1, 3, 4, 8, 9, 11-16 Claims 1, 3, 4, 9, or 11-15 inclusive to a patient having arthritis.

Claim 38 (currently amended). A method for treating according to Claim 37, charactherized characterized in that the disease is osteoarthritis.

Claim 39 (currently amended). A method for treating according to Claim 37, charactherized characterized in that the disease is rheumatoid arthritis.